

breaths quickly. The first two are exhaled and the third is held while the patient bears down. If the pain is more severe, more breaths can at once be taken, but we find this is usually sufficient. If the patient is susceptible to nitrous oxid more oxygen can be given. If the pain is a long one a single additional breath of the same mixture can be taken and held while the patient pushes, and a third single breath in like manner. We use the high percentage of oxygen for the sake of the baby, which in utero is susceptible to nitrous oxid, but with the percentage of oxygen mentioned, no injury to the baby's heart or respiratory center will occur. As soon as the head is born pure oxygen is given until the baby is born and is pink, provided the cord is still pulsating. Recently a baby became blue about a minute after it was born, oxygen having been stopped in the meantime. As the cord was still pulsating the mask was again put on the patient's face and all cyanosis in the baby disappeared after the mother had taken a few breaths of oxygen, the baby not breathing meanwhile. Results are not always quite as striking as this. Besides protecting the baby the percentage of oxygen we use is safe for the mother, even if labor is complicated by toxemias or some chest condition.

During the influenza epidemic we were occasionally called upon to give nitrous oxid to an influenza patient in labor. In some cases we added more oxygen than our usual 20 per cent. This was especially true of a few pneumonia cases. One case is worth mentioning in this connection. The patient was dangerously ill with influenza pneumonia. The case was a breech presentation, and nitrous oxid-oxygen was given. Fifty per cent oxygen was used for pains and 30 per cent during delivery, with two minutes pure oxygen as soon as the baby was born. The patient was returned to bed in better condition than she had been before delivery, and made a good recovery. In this case the large percentage of oxygen given was probably instrumental in tiding the patient over a period of anoxemia, which experimenters have shown may be sufficient to determine the favorable outcome of a pneumonia or at least hasten it.

In Caesarean sections we also add about 20 per cent oxygen to the nitrous oxid, preferring to use a minute amount of added ether vapor rather than decrease the oxygen. Frequently, when the baby is delivered we give pure oxygen for the short interval until the cord is clamped. This is not long enough to allow the patient to awaken. In almost every case the child cries as soon as removed from the uterus.

CONCLUSION

The three physicians on the regular anesthetic staff at Stanford hospital have had ample opportunity, during the average of about 3000 cases a year, given or supervised by them, to compare the clinical differences of patients receiving oxygen and those not given any. In general these anesthetists have independently reached the conclusion that, besides the advantages just noted, an oxygen-ether anesthesia will usually be smoother, more even, with the use of considerably less ether to keep the

patient asleep than is necessary when a plain ether anesthesia is given. Their clinical observations verify the advantages noted by the many experimenters of late years who have tested the value of oxygen. Various definite tests and experiments have been planned, but not undertaken. I can only say that in actual practice during many years of use we find most patients under anesthesia do better with oxygen out of all proportion to anything we so far know as the cause.

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THE DIAGNOSIS AND CURE OF GONORRHEA

A COMPARATIVE STUDY OF SMEARS, CULTURES, AND COMPLEMENT FIXATION METHODS *

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The mooted question of the cure of gonorrhea seems by these investigations to be divided into two stages: (1) The cessation of infectivity, and (2) the subsidence of clinical signs and symptoms.

Many varying standards have been suggested for the determination of cure. Harrold bases his conclusions upon the cultivation of the gonococcus, provocative and serological tests. Fraser sets very reasonable and easily attained standards, including disappearance of symptoms, examination, observation, provocative vaccines and sounds, with a plea against overtreatment. Clarkson devises a very comprehensive set of tests. Rosenthal describes a set of tests which are well within the resources of anyone.

The British Medical Research Committee finds that "the stage has not yet been reached at which a diagnosis can be made with certainty. . . by bacteriological methods alone."

The committee on medical research and laboratory questions of the all-American conference on venereal disease which met at Washington December 6 to 11, 1920, feeling the need of further scientific knowledge on the subject, urged the conference to encourage research work along the lines of diagnosis.

With the object of simplifying the various criteria offered by the different observers and placing them on as nearly a measurable basis as possible, we attempted to devise practical standards. The material studied comprised several hundred cases of acute and chronic urethritis, the last 100 observations having been used for critical study.

The factors considered were history, appearance of smears stained by methylene blue, and the Gram method at two laboratories working independently, cultures on various media and the complement fixation tests. It is realized that for a test to be of great value it must be simple enough to encourage its frequent application. Everyone has noted elaborate tests offered for diagnosis, which are so com-

* Presented before the Urology Section at the annual meeting in Yosemite.

plicated as to render them not practicable for regular use.

It would appear that the presence of a few gonococci, apt to be overlooked in the examination of smears, could be vastly magnified by successful cultures. Until comparatively recently the cultivation of the gonococcus has been looked upon as an extremely difficult procedure, available only to the most skilful laboratory workers. Wheery and Oliver, however, discovered that the gonococcus can be grown well under reduced oxygen tension. This they accomplished by culturing *B. Subtilis* opposite the gonococcus, using top and bottom of Petri dishes. Schwartz simplifies this method, making the growth of the gonococcus almost as easy as that of any other organism. The method will be described later in detail.

Our method of attack was to start with frank gonorrheas in either sex, and, verifying this with stained smears, to persist until positive cultures were got in nearly all instances; having arrived at this point to determine at what time the gonococci could no longer be cultivated and combining with this the complement fixation tests. Finally cases at all stages were subjected to these tests.

ROUTINE

All smears were made in triplicate. If a spontaneous discharge was present, care was taken to wipe off that which was exposed and to insert the platinum loop well into the urethra or cervix. If there was no discharge, it was produced by gently stripping the urethra. In the male, if this produced no visible amount, the prostate and seminal vesicles were massaged.

All smears were spread on slides as thinly as possible, air dried and fixed by three rapid passes through the flame. It is of advantage to make smears at either end of the slide, thus saving time and slides.

If, upon staining with methylene blue, intracellular diplococci were found, a Gram stain was made by two laboratories working independently. The following technic for Gram staining was found satisfactory:

1. Stirling's gentian violet, one-fourth minute, wash with water.
2. Gram's iodine, one minute, wash with water.
3. Ethyl alcohol (95 per cent) until thoroughly decolorized—about two minutes, wash with water.
4. Safranine (approximately one part saturated alcoholic solution to seven parts of aqua distillata) one-half minute, wash with water.
5. Blot almost dry and heat gently to dryness.

For culturing, various media were tried. Hydrocele, pleural, ascitic, human blood and horse serum agar were used with apparently equally good results. We finally settled upon ascitic agar as the most easily obtained. The method of preparation of this is as follows:

Five hundred grams of fresh lean meat (veal or beef) is finely minced and thoroughly mixed with 1000 cc. of distilled water. This mixture is allowed

to stand on ice for twenty-four hours. The liquor is then decanted and the remainder expressed through cloth, adding enough distilled water to make 1000 cc. Boil until the albumin of the meat infusion coagulates. Correct to an acidity of pH 7.6 by the use of N/10 NaOH. Titrate at close to 100° C., to eliminate effect of carbon dioxide. Boil again for a short time, filter and make up to 1000 cc. with distilled water. Add 10 grams peptone (Bacto. Difco.), 5 grams NaCl (C. P.) and 20 grams agar, and boil until all is dissolved. Let cool to 50° C., add whites of three fresh eggs and clarify by filtration, or filter and refilter through absorbent cotton until media are clear. Tube the media and autoclave at ten pounds on three consecutive days. Melt the agar, cool to 50° C., add sterile hydrocele fluid in the proportion of 1 cc. of fluid to 2 cc. of agar. Slant and stopper with sterile rubber stoppers.

Cultures are made as follows:

The glans penis in the male or the tissue surrounding the urethra and cervix in the female are carefully sponged with mercury cyanide 1/1000, the platinum loop introduced well into the urethra and smeared over the agar slants, the operation being repeated.

This mode of inoculation gives discrete colonies, the identification of which is easier than when the liquid at the bottom of the tube is inoculated and the whole flowed over the surface. Culture medium is kept in the incubator before the inoculation, which insures its being sterile and at the best temperature at all times. If cultures are to be made away from the laboratory, the test tubes containing the medium are placed in hot water (98-100°) until thoroughly heated. After the inoculation they are kept warm until placed in the incubator. The oxygen tension is reduced according to the method described by Schwarz by rotating the test tube in the flame of a Bunsen burner until it has been thoroughly heated, stoppering it and placing at once in the incubator, which is maintained at 37.5° C.

Care must be taken that the tube be not heated sufficiently to crack it or to destroy the culture. Tightly fitting rubber stoppers are used, and if they happen to be moist, by observing the film between the stopper and the tube, one can sometimes detect air leaks as the tube cools. Failure to accomplish a suitable growth is sometimes due to these leaks and has been overcome in our experience by reheating the tube, which subsequently showed a luxuriant growth. Cultures are inspected at twenty-four and forty-eight hours; at the latter time they are usually ready for study. Criteria used in examining the cultures are the shape of the colonies, morphology of the organisms and staining characteristics, using standard gram negative and positive organisms for control.

TABLE NO. ONE
PER CENT OF POSITIVE FINDINGS IN KNOWN POSITIVES DURING ACUTE STAGE

No. Cases	History	Gram Stains		Cultures	Complement Fixation	Other Findings
		No. 1	No. 2			
36	97%	83%	92%	58%	5.5%	
8*	100%	0	0	0	0	Chronic Prostatitis of Gonorrheal Origin Pus cells and reduced lecithin in prostatic and seminal secretions.
15	100%	0	0	0	0	Re-examination of Former Gonorrheas Cultures showed staphylococci, diptheroids and a gram negative bacillus.
21	0	0	0	0	0	Non-specific Urethritis

* Including one stricture.

TABLE NO. TWO
TIME OF DISAPPEARANCE OF POSITIVE FINDINGS

Case No.	History	Smrs.	Cltre.	Complement Fixation	Notes
76	Acute Urethritis Cervicitis.	5 Days	5 Days	XXX after 4 Days	C. F. Fluctuated between XX and XXX for 70 days; negative after 88 Days. Diphtheroids and Staphylococci present.
83	Acute Anterior Urethritis	See Note		Always Negative	Disappeared in smears and cultures after 12 days; reappeared in smears after 20 days. Staphylococci.
94	Chronic Anterior Urethritis	17 Days	17 Days	Always Negative	Urethral discharge still present. Staphylococci.
2	Ditto	30 Days	30 Days	Positive at 24 Days; negative thereafter	Urethral discharge still present. Staphylococci and Streptococci.
96	Ditto	31 Days	20 Days	Always Negative	Urethral discharge present after 54 days. Diphtheroids and Staphylococci.
14	Chronic Anterior Urethritis	37 Days	Never Positive	Always Negative	Urethral discharge still present. Staphylococci.
73	Acute Anterior Urethritis and Epididymitis	60 Days	60 Days	Always Negative	This case beyond observation between cultures. Staphylococci.
23	Acute Anterior Urethritis	70 Days	58 Days	Always Negative	Auto infection following drinking bout. Staphylococci and Diptheroids.
87	Ditto	45 Days	45 Days	Always Negative	This case beyond observation between cultures. Staphylococci.
60		35 Days	33 Days	Always Negative	Staphylococci and Diptheroids.
88		Present, urethra and cervix after 35 days		Always Negative	Staphylococci and spore forming bacilli.
93		Present 124 days after 276 Days		Always Negative in spite of Vaccines	Infection of the Periurethral Glands. Diptheroids and Staphylococci.

Table No. 1 contains the findings in the various cases.

In thirty-six, during the acute stage, 97 per cent gave positive histories. Gram negative intracellular diplococci were found in 83 to 92 per cent, depending upon the technician, or in 100 per cent if combined. Gonococci were successfully cultivated in 58 per cent. Complement fixation was positive in 5.5 per cent. In eight cases, including one of stricture, all search for gonococci by smears or cultures were negative, though the prostatic and vesicular secretions contained pathological amounts of pus and reduced lecithin granules. Bacteriologically, these contained staphylococci, small gram negative bacilli and diptheroid bacilli.

Fifteen cases, apparently cured, on re-examination showed entirely negative findings except that bacteriologically they were as above.

Twenty-one cases of non-specific urethritis and vaginitis also showed the same organisms. All of these organisms were not present simultaneously nor in all cases.

Table No. 2 shows the time of disappearance of positive findings after the beginning of treatment.

This varies in the smears from five to seventy days, with one case of littritis in which it has persisted for over 276 days.

In the cultures we have got successful growths up to 124 days after beginning treatment. The average time (excluding incompleated cases) for the disappearance of gram negative intracellular diplococci is slightly longer than that for getting successful cultures. In no instance with patients under treatment was it possible to get cultures of gonococci after the gram negative diplococci had disappeared from the stained smear. The complement fixation test (in this series of cases at least) was of little value.

Notwithstanding the fact, however, that cultures and smears were negative, the patients were definitely not cured. There were still heavy urinary shreds or urethral discharge or both present. This, perhaps, justifies our opening statement, that the cure should be divided into two stages.

There may be those who would say at this time that the patients are not infective. It has happened, in our observation, that patients have been completely negative to smear and culture and be-

come positive again. This was noted in case 83, which was negative as to smears and cultures in twelve days. After physical exertion the smears became positive again in twenty-six days, remaining so for days.

What it is that serves to perpetuate discharges from the anterior urethra or pus in the prostate or seminal vesicle after the disappearance of gonococci we are at this time not prepared to state, but it is suggestive that staphylococci were present in the majority of cases after disappearance of gonococci, as also in the non-specific urethritis cases in which no other pathology was found.

What, then, shall we place as the criteria for cure?

1. Absence of all urethral discharge.
 2. Urines, 1, 2 and 3, free from shreds; or if they be present, the shreds free from pus cells. (The All-American Conference considers shreds not important if they float for at least two minutes after agitating the fluid.)
 3. Frequency of urination normal with no nocturia.
 4. Prostate and seminal vesicles normal to palpation and free from pus cells. Lecithin present in prostatic secretions in normal amounts.
- In many instances it is virtually impossible to obtain the desired degree of freedom from pus cells in these secretions. Cessation of treatment followed by a normal sexual life for a few months will usually clear up these remaining pus cells.
5. As the patient is being prepared for dismissal, sounds should be passed to determine the patency of the urethra and for their therapeutic effect. If this is done gradually, it will not be followed by a discharge.
 6. Discharge following silver nitrate, if any, negative microscopically and bacteriologically to gonococci.
 7. Testicles, epididymes and vasa should be normal.
 8. Physical exertion should not produce discharge; neither should the injection of vaccines.

Endoscopy immediately after cessation of treatment is apt to give unsatisfactory results, unless one bears in mind the fact that treatment over the delicate mucus membrane of the urethra, together with the preceding infection, is very apt to develop a picture susceptible of misinterpretation. In this, one finds varying degrees of congestion and alteration of the normal striations. During endoscopy, it is well to palpate the entire surface of the urethra for spots of infiltration. Subsequent examinations at three, six, and nine months should establish the importance of any residual findings at previous examinations.

CONCLUSIONS

1. The cultivation of the gonococcus can be done as simply as that of any other organism, providing the medium is warmed before inoculating and kept warm until the oxygen tension has been reduced and the tube transferred to the incubator.
2. Ability to cultivate the gonococcus seems to

disappear first under treatment, and seldom has reappeared. The finding of gram negative intracellular diplococci is the second factor to disappear; the subjective and objective findings persist very much longer, and the patient cannot be considered to have been cured until they have been entirely eliminated. Despite favorable comment in the literature, we cannot attach much more favorable conclusion to the value of the complement fixation test than those drawn by Krotoszyner in February, 1918.

PROPORTION OF PHYSICIANS TO POPULATION

State	Population (1920)	Physicians* (1922)	People to each Physician
Alabama	2,348,174	2,313—	1,015
Arizona	333,903	372—	897
Arkansas	1,752,204	2,303—	760
California	3,426,861	7,549+	454
Colorado	939,629	1,822+	499
Connecticut	1,380,631	1,727—	799
Delaware	223,003	265+	842
District of Columbia	437,571	1,924+	227
Florida	968,470	1,348+	718
Georgia	2,895,832	3,274—	885
Idaho	431,866	452—	956
Illinois	6,485,280	10,716+	605
Indiana	2,930,390	4,353—	673
Iowa	2,404,021	3,490—	689
Kansas	1,769,257	2,492—	709
Kentucky	2,416,630	3,155—	766
Louisiana	1,798,509	2,058+	874
Maine	768,014	1,067—	718
Maryland	1,449,661	2,349—	616
Massachusetts	3,852,356	5,977+	645
Michigan	3,668,412	4,653+	788
Minnesota	2,387,125	2,774+	860
Mississippi	1,790,618	1,792+	999
Missouri	3,404,055	5,827—	584
Montana	548,889	568—	966
Nebraska	1,296,372	1,913—	678
Nevada	77,407	140—	553
New Hampshire	443,083	615—	720
New Jersey	3,155,900	3,362+	939
New Mexico	360,350	399—	903
New York	10,384,829	16,857+	616
North Carolina	2,559,123	2,226—	1,149
North Dakota	645,680	517—	1,248
Ohio	5,759,394	8,086—	712
Oklahoma	2,028,283	2,600—	779
Oregon	783,389	1,158+	677
Pennsylvania	8,720,017	11,241—	775
Rhode Island	604,397	754—	801
South Carolina	1,683,724	1,368—	1,231
South Dakota	636,547	630—	1,010
Tennessee	2,337,885	3,228—	724
Texas	4,663,228	6,094—	765
Utah	449,396	497+	904
Vermont	352,428	556—	634
Virginia	2,309,187	2,503—	918
Washington	1,356,621	1,756—	772
West Virginia	1,463,701	1,751—	836
Wisconsin	2,632,067	2,772+	950
Wyoming	194,402	263—	739
Totals	105,708,771	145,966+	724

* The plus and minus signs indicate, respectively, an increase or a decrease in the number of physicians in the State since 1920.